CLAIMS

What is claimed is:

1. A method for transducing host cells comprising:

a) providing:

i) at least one host cell comprising a genome, and

ii) a plurality of retroviral vectors encoding a gene of interest; and

b) contacting said at least one host cell with said plurality of integrating vectors under conditions such that said host cells are transduced to produce transduced host cells;

c) repeating steps a) and b) a plurality of times to provide host cells comprising multiple integrated retroviral vectors.

2. The method of Claim 1, wherein steps a and b are repeated at least 3 times.

3. The method of Claim 1, wherein steps a and b are repeated at least 4 times.

4. The method of Claim 1, wherein steps a and b are repeated at least 5 times.

5. The method of Claim 1, wherein steps a and b are repeated at least 6 times.

6. The method of Claim 1, wherein steps a and b are repeated at least 7 times.

7. The method of Claim 1, wherein steps a and b are repeated at least 8 times.

8. The method of Claim 1, wherein steps a and b are repeated at least 10 times.

9. The method of Claim 1, wherein steps a and b are repeated at least 20 times.

10. The method of Claim 1, wherein steps a and b are repeated between about 3 and 20 times.

11. The method of Claim 1, wherein said host cells comprising multiple integrated vectors comprise between about 10 and about 100 integrated retroviral vectors.

12. The method of Claim 1, wherein said retroviral vectors utilized in steps 1 and 2 are produced from packaging cells transfected with an envelope plasmid and a vector plasmid.

13. The method of Claim 1, further comprising step:

d) transducing said host cells comprising multiple integrated retroviral vectors produced by steps 1 and 2 with vectors produced from packaging cells produced by transducing said packaging cells with a retroviral vector encoding said gene of interest and transfecting said packaging cell with a plasmid expressing an envelope protein.

14. The method of Claim 12, wherein said packaging cells express retroviral gag and pol proteins.

15. The method of Claim 14, wherein said packaging cells are 293-GP cells.

16. The method of Claim 12, wherein said envelope plasmid encodes a G protein.

17. The method of Claim 16, wherein said G protein is VSV-G protein.

18. The method of Claim 1, wherein said retroviral vector comprises MoMLV elements.

19. The method of Claim 1, wherein said conditions comprise contacting said host at a multiplicity of infection of from about 10 to 1000.

20. The method of Claim 1, wherein said gene of interest is operably linked to an exogenous promoter.

21. The method of Claim 1, wherein gene of interest is operably linked to a signal sequence.

22. The method of Claim 1, wherein said retroviral vector encodes at least two genes of interest.

23. The method of Claim 22, wherein said at least two genes of interest are arranged in a polycistronic sequence.

24. The method of Claim 23, wherein said at least two genes of interest comprise immunoglobulin heavy and light chains.

25. The method of Claim 1, wherein said retroviral vector is a lentiviral vector.

26. The method of Claim 1, wherein said host cell is selected from Chinese hamster ovary cells, baby hamster kidney cells, human 293 cells, and bovine mammary epithelial cells.

27. The method of Claim 1, further comprising clonally selecting said transduced host cells.

28. The method of Claim 27, further comprising culturing said clonally selected host cells under conditions such that a protein of interest encoded by said gene of interest is produced.

29. The method of Claim 1, wherein said integrating vector further comprises a secretion signal sequence operably linked to said exogenous gene.

30. The method of Claim 28, further comprising isolating said protein of interest.

31. The method of Claim 28, wherein said culture conditions are selected from the group consisting of roller bottle cultures, perfusion cultures, batch fed cultures, and petri dish cultures.

32. The method of Claim 28, wherein said host cells synthesize greater than about 1 picograms per cell per day of said protein of interest.

33. The method of Claim 28, wherein said host cells synthesize greater than about 10 picograms per cell per day of said protein of interest.

34. The method of Claim 28, wherein said host cells synthesize greater than about 50 picograms per cell per day of said protein of interest.

35. The method of Claim 1, wherein said retroviral vector further encodes an amplifiable marker.

36. The method of Claim 35, wherein said amplifiable marker is selected from the group consisting of DHFR and glutamine synthetase.

37. The method of Claim 35, further comprising the step of culturing said transduced host cells under conditions that allow for amplification of the integrated retroviral vectors.

38. The method of Claim 37, wherein said conditions comprise culturing said transduced host cells in the presence of a selection agent selected from the group consisting of methotrexate, phosphinothricin and methionine sulphoxime.

39. The method of Claim 24, wherein said immunoglobulins are selected from the group consisting of IgG, IgA, IgM, IgD, IbE and sIg.

40. The method of Claim 1, wherein said host cell is transduced with at least two different vectors encoding different genes of interest.

41. A host cell produced by the method of Claim 1.

42. A method for transducing host cells comprising:

a) providing:

i) providing at least one host cell comprising a genome, and

ii) a plurality of retroviral vectors encoding a gene of interest; and

b) contacting said at least one host cell with said plurality of integrating vectors under conditions such that said host cells are transduced to produce transduced host cells;

c) repeating steps 1) and 2) a plurality of times to provide host cells comprising multiple integrated retroviral vectors;

d) clonally selecting a host cell expressing said gene of interest; and

e) purifying a protein of interest encoded by said gene of interest.